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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,222	06/23/2006	Takehisa Iwama	292353US0X PCT	1696

22850 7590 10/02/2007

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EXAMINER	
POLANSKY, GREGG	
ART UNIT	**PAPER NUMBER**
1614	

NOTIFICATION DATE	DELIVERY MODE
10/02/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/584,222	IWAMA ET AL.	
	Examiner	Art Unit	
	Gregg Polansky	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicants' preliminary amendment, filed 6/23/2006, amending Claim 5, is acknowledged.

2. Applicants' Information Disclosure Statement, filed 6/23/2006, is acknowledged and has been reviewed.

3. Claims 1-5 are pending.

4. Claims 1-5 are under consideration.

5. Claims 1-5 are being examined as claims drawn to compositions (i.e., pharmaceutical agents).

Specification

6. Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 5 does not further limit the subject matter of Claim 1. Claim 5 recites an intended use. The recitation of intended use does not further limit a claim drawn to a composition. *In re Hack*, 114 USPQ 161.

Claim Rejections - 35 USC § 112 Second Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 recite the limitation of "A is a C_{1-5} alkylene which **may** be substituted with a hydroxyl group" (emphasis added), resulting in claims that do not clearly set forth the metes and bounds of the patent protection desired. Applicants must specifically recite all substituents contemplated.

Claim Rejections - 35 USC § 112 First Paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating COPD, does not reasonably provide enablement for preventing COPD. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a

single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to the prevention and treatment of COPD.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The National Heart Lung and Blood Institute's "Diseases and Conditions Index" information on COPD teaches that the causes of COPD include, cigarette smoking, exposure to secondhand smoke, prolonged inhalation of chemical fumes, working in a dusty area over many years, heavy exposure to air pollution, and genetic disorders (e.g., alpha 1 antitrypsin deficiency). COPD may also result from lung damage caused by frequent and severe lung infections (*see* pages 4-5). COPD includes emphysema and chronic bronchitis. Although smoking is the leading cause of COPD, only about 15% of smokers develop the disease (*see* The Merck Manuals Online Medical Library, "Chronic Obstructive Pulmonary Disease", page 2). This is one indicator of the unpredictability of the art.

Since there are numerous causes of COPD, and it is impossible to predict who will be affected by COPD, prevention is not possible. Even with the elimination of exposure to all environmental causes of COPD, COPD may still occur (e.g.

genetic diseases). Any theoretical preventative treatment would require treating everyone.

(5) The relative skill of those in the art:

The relative skill of those in the art is that of a medical doctor or a Ph.D. Pharmacologist.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for treating the neutrophilia associated with COPD, as demonstrated by a dose dependent decrease in neutrophils in a guinea pig respiratory dysfunction model (i.e., airway neutrophilia induced by exposure to tobacco smoke was inhibited by administration of a compound recited in Claim 3 (4-bromo-6-[3-(4-chlorophenyl)propoxy]-5-(3-pyridylmethylamino)-3(2H)-pyridazinone hydrochloride)).

However, the specification does not provide a method for <u>preventing</u> COPD.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regard to many causes and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Egi et al. (U.S. Patent 6,284,758).

Egi et al. teach the structural formula (formula (I)), substituents, and pharmaceutically acceptable salt thereof of instant Claim 1, in pharmaceutical formulations (*see* column 4, lines 11-38, and formula (I), column 1, lines 35-46). Egi et al. teach the substituents recited in instant Claim 2 (*see* column 10, claim 2). Egi et al. also teach both compounds recited in instant Claim 3 – that is, 4-bromo-6-[3-(4-chlorophenyl)propoxy]-5-(3-pyridylmethylamino)-3(2H)-pyridazinone (*see* column 3, lines 17-18) and 4-bromo-6-[3-(4-chlorophenyl)-3-hydroxypropoxy]-5-(3-pyridylmethylamino)-3(2H)-pyridazinone (*see* column 3, lines 26-27). Additionally, Egi et al. teach organic acid salts or inorganic acid salts of the disclosed compounds, as is recited in instant Claim 4 (*see* column 3, lines 41-45). The reference also teaches the formulation of the compound into tablets, capsules, ointments, and aerosol suspensions (*see* columns 8-9, Examples 1-4).

Note that a composition comprising the same ingredient as the claimed composition, will inherently possess the qualities recited herein.

It is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

Therefore, Egi et al. teach all of the limitations of instant Claims 1-5.

13. Claim 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Tanikawa et al. (U.S. Patent 5,314,883).

Claim 14 of Tanikawa et al. (*see* column 62) teach the formulation (composition) 4-bromo-6-[3-(4-chlorophenyl)propoxy]-5-(3-pyridylmethylamino)-3(2H)-pyridazinone and its pharmaceutically acceptable salt, which is one of the two compounds recited by instant Claim 3.

See the discussion on intended use and inherency discussed above.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claim s1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doherty et al. (U.S. Patent 6,037,346).

Doherty et al. teach 4-bromo-6-[3-(4-chlorophenyl)propoxy-5-(3-pyridylmethylamino)-3(2H)-pyridazinone and its pharmaceutically acceptable salt, a compound recited in instant Claim 3 , and defined by formula (I) of instant Claim 1, is a type V phosphodiesterase inhibitor (*see* column 8, lines 6-9 and lines 33-67). Doherty et al. teach that this compound (and other phosphodiesterase inhibitor compounds disclosed in the reference) is useful in a method to treat erectile dysfunction. Doherty et al. also teach that phosphodiesterase inhibitors have other therapeutic uses including, *inter alia*, treatment of obstructive lung disease (*see* column 3, lines 1-6).

Although Doherty et al. do not teach the use of the instant compound described above for the treatment of COPD, they do teach that the compound is a phosphodiesterase inhibitor, and that phosphodiesterase inhibitors are effective in the treatment of obstructive lung disease (*supra*).

It would be obvious to one of ordinary skill in the art, at the time of the invention, to combine the teaching of Doherty et al. (i.e., phosphodiesterase inhibitors are effective in the treatment of obstructive lung disease and 4-bromo-6-[3-(4-chlorophenyl)propoxy-5-(3-pyridylmethylamino)-3(2H)-pyridazinone is a phosphodiesterase inhibitor). These disclosures by Doherty et al. would also motivate the artisan to use the compound in patients with COPD.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-5 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-6 and 14 of U.S. Patent No. 5,314,883. Although the conflicting claims are not identical, they are not patentably distinct from each other because they all recite compositions/"agents" that read on the compositons/"agents" recited in the instant claims.

Conclusion

20. Claims 1-5 are rejected.

21. No claims are allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregg Polansky whose telephone number is (571) 272-9070. The examiner can normally be reached on Mon-Thur 8:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GP

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER

9/26/07